



## Complete Summary

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### **GUIDELINE TITLE**

Bronchioloalveolar lung cancer: ACCP evidence-based clinical practice guidelines.  
(2nd Edition)

### **BIBLIOGRAPHIC SOURCE(S)**

Arenberg D, American College of Chest Physicians. Bronchioloalveolar lung cancer: ACCP evidence-based clinical practice guidelines (2nd edition). Chest 2007 Sep;132(3 Suppl):306S-13S. [63 references] [PubMed](#)

### **GUIDELINE STATUS**

This is the current release of the guideline.

## COMPLETE SUMMARY CONTENT

SCOPE  
METHODOLOGY - including Rating Scheme and Cost Analysis  
RECOMMENDATIONS  
EVIDENCE SUPPORTING THE RECOMMENDATIONS  
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## SCOPE

### **DISEASE/CONDITION(S)**

Bronchioloalveolar lung cancer

### **GUIDELINE CATEGORY**

Diagnosis  
Treatment

### **CLINICAL SPECIALTY**

Family Practice  
Oncology  
Pulmonary Medicine

Radiation Oncology  
Thoracic Surgery

## **INTENDED USERS**

Advanced Practice Nurses  
Allied Health Personnel  
Health Care Providers  
Nurses  
Patients  
Physicians  
Psychologists/Non-physician Behavioral Health Clinicians  
Social Workers

## **GUIDELINE OBJECTIVE(S)**

To review the current evidence on special issues relating to the diagnosis, imaging, prognosis, and treatment of bronchioloalveolar carcinoma (BAC)

## **TARGET POPULATION**

Patients with known or suspected "pure bronchioloalveolar carcinoma (BAC)" as defined in the 1999 World Health Organization (WHO) revised classification for lung tumors

## **INTERVENTIONS AND PRACTICES CONSIDERED**

### **Diagnosis**

1. Revised World Health Organization (WHO) classification system for accurate diagnosis of bronchioloalveolar carcinoma (BAC)
2. Surgical biopsy
3. If no biopsy, diagnosis of BAC needs compatible histopathologic pattern on transbronchial or core needle biopsy and a computed tomography (CT) demonstrating a pure ground-glass or pneumonic appearance
4. Additional diagnostic testing with negative positron emission tomography (PET)

### **Treatment**

1. Standard chemotherapy
2. First-line epidermal growth factor receptor (EGFR)-targeted agents

## **MAJOR OUTCOMES CONSIDERED**

Survival

## **METHODOLOGY**

## **METHODS USED TO COLLECT/SELECT EVIDENCE**

Hand-searches of Published Literature (Primary Sources)  
Searches of Electronic Databases

## **DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE**

### **Overview**

The American College of Chest Physicians (ACCP) chose the Duke University Center for Clinical Health Policy Research to perform formal systematic reviews of the current evidence in the five new non-small cell lung cancer (NSCLC) topic areas, as well as to provide a search for the existing guidelines, systematic reviews, and meta-analyses in all of the topics areas. In addition, the Agency for Healthcare Quality and Research (AHRQ) agreed to fund the BlueCross BlueShield Association Technology Evaluation Center to perform the formal systematic review of literature on small cell lung cancer (SCLC). The Health Outcomes Research Group of the Department of Epidemiology and Biostatistics at Memorial Sloan-Kettering Cancer Center conducted a full-scale review of the literature since the first set of guidelines in the area of screening for lung cancer to assist that particular writing group.

The formal systematic reviews of the five new topic areas were guided by the appropriate chapter editors and their writing committees, in concert with the Executive Committee of the panel.

The two EPC research teams conducted a variety of systematic computerized bibliographic database searches including the following: (1) a search for systematic reviews, guidelines, and meta-analyses published since the last ACCP lung cancer guideline (MEDLINE, The Cochrane Library, National Guidelines Clearinghouse); (2) targeted searches for reviews in each of five selected treatment sections (solitary pulmonary nodules, stage I and II, stage IIIA, stage IIIB, stage IV); these searches, run in OVID version of MEDLINE, were performed in July and August 2005 and were limited to publication years since 1995, English language, and human subjects; and (3) searches related to SCLC are described in the evidence chapter on SCLC. Search terms included the medical subject heading terms lung neoplasms (exploded) and bronchial neoplasms for the lung cancer concept. Each topic search utilized key words specific to the key questions of interest (complete search strategies are available on request from the authors).

### **Strategy Specific for Bronchioloalveolar Carcinoma (BAC)**

The clinical questions in this guideline were chosen to focus on areas in which there are important differences between BAC and other forms of NSCLC. These guidelines are restricted to patients with known or suspected "pure BAC" as defined in the 1999 World Health Organization (WHO) revised classification for lung tumors. This classification system requires that the term bronchioloalveolar carcinoma be reserved for a more narrowly defined histologic appearance of cells growing in a lepidic pattern with no stromal, vascular, or pleural invasion. Articles dealing with the prognosis, treatment, and positron emission tomography (PET) characteristics of BAC were chosen from literature searches. Many articles were selected for review on the basis of their presence in the bibliographies of initially selected papers. Meeting abstracts were searched from the last 5 years of meetings of the American Society of Clinical Oncology. Except when needed to

illustrate differences over time, articles were chosen preferably when published after 1999 to reflect data using the most current WHO definition of BAC.

## **NUMBER OF SOURCE DOCUMENTS**

Not stated

## **METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE**

Expert Consensus  
Weighting According to a Rating Scheme (Scheme Given)

## **RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE**

**High** Randomized controlled trials (RCTs) without important limitations or overwhelming evidence from observational studies\*

**Moderate** RCTs with important limitations (inconsistent results, methodologic flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies\*

**Low or very low** Observational studies or case series

\*Although the determination of magnitude of the effect based on observational studies is often a matter of judgment, the guideline developers offer the following suggested rule to assist this decision: a large effect would be a relative risk  $>2$  (risk ratio  $< 0.5$ ) [which would justify moving from weak to moderate], and a very large effect is a relative risk  $> 5$  (risk ratio  $< 0.2$ ) [which would justify moving from weak to strong]. There is some theoretical justification in the statistical literature for these thresholds (the magnitude of effect that is unlikely or very unlikely to be due to residual confounding after adjusted analysis). However, once the decision is made, authors should be explicit in justifying their decisions.

## **METHODS USED TO ANALYZE THE EVIDENCE**

Review of Published Meta-Analyses  
Systematic Review

## **DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE**

Quality of evidence is scored in three categories with high-quality evidence obtained from randomized controlled trials (RCTs) without important methodologic limitations based on the study design, the consistency of the results, and the directness of the evidence. In extraordinary circumstances, significant and consistent evidence from observational studies could also be ranked as high quality. RCTs with important methodologic limitations or flaws, inconsistent results, or indirect or imprecise results would be scored as medium quality, as well as exceptionally strong evidence from observational studies. Other observational studies or case-series data would fall into the low quality of evidence category. It is the interface of the quality of the evidence and the balance of benefits to harms or burdens that determines the strength of the

recommendation, with a 1A recommendation being the strongest and 2C the weakest.

## **METHODS USED TO FORMULATE THE RECOMMENDATIONS**

Expert Consensus  
Informal Consensus

## **DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS**

Writing committees studied the evidence and summary tables or reviewed the literature for their assigned topics, developing their arguments for the recommendations and suggested grading of those recommendations that were put forth for early drafts. The Executive Committee of the panel, composed of the Chair, Vice-Chair, methodologist, and both project managers, reviewed drafts of each chapter of the manuscript during the writing process. Sections that were determined to be potentially overlapping were shared among the appropriate chapter editors, and conference calls were organized to coordinate the placement of these sections and to confirm that there would be no conflicting information or recommendations.

A conference of the panel was convened in July 2006, prior to which time all panelists, including representatives from the invited organizations, were requested to review the complete manuscript and identify recommendations for which the proposal, wording, or grading were determined to be controversial or could be interpreted as controversial by others, incorrectly evolved from the evidence, disagreement existed with regard to the proposal or the grading, or required full panel discussion and further review for any reason. When the panelists who were present were not in unanimous agreement with the proposed recommendations or the grading of the recommendations, informal group consensus techniques were employed. After the meeting, a series of conference calls were convened to finish the discussions and finalize the recommendations. There were a few chapters for which there was insufficient time for full dialogue during the meeting; in the interest of ensuring that the recommendations followed the evidence, the conference calls were necessary. This process ensured the "buy-in" of the panelists and was deemed to be a worthwhile effort.

## **RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS**

### **Grade of Recommendations Scale**

| <b>Grade</b> | <b>Recommendation</b> |
|--------------|-----------------------|
| 1A           | Strong                |
| 1B           | Strong                |
| 1C           | Strong                |
| 2A           | Weak                  |
| 2B           | Weak                  |
| 2C           | Weak                  |

## Relationship of Strength of the Supporting Evidence to the Balance of Benefits to Risks and Burdens

| Balance of Benefits to Risks and Burdens |                                 |                                 |                 |           |
|--|---------------------------------|---------------------------------|-----------------|-----------|
| Quality of Evidence                      | Benefits Outweigh Risks/Burdens | Risks/Burdens Outweigh Benefits | Evenly Balanced | Uncertain |
| High                                     | 1A                              | 1A                              | 2A              |           |
| Moderate                                 | 1B                              | 1B                              | 2B              |           |
| Low or very low                          | 1C                              | 1C                              | 2C              | 2C        |

### COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

### METHOD OF GUIDELINE VALIDATION

Peer Review

### DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Following final chapter revisions and incorporation of these ultimate recommendations and grading, a concluding review was conducted by the guideline panel Executive Committee. The guidelines were then submitted for review and approval to the American College of Chest Physicians Health and Science Policy Committee (ACCP HSP) Committee, as well as the Thoracic Oncology Network of the college.

## RECOMMENDATIONS

### MAJOR RECOMMENDATIONS

Definitions for the strength of evidence and recommendation grades (1A-2C) follow the recommendations.

1. The guideline developers recommend that the use of the term *bronchioloalveolar carcinoma* (BAC) be reserved for lung cancers that meet the criteria established in the revised World Health Organization (WHO) classification system for lung tumors. **Grade of recommendation, 1B**
2. For patients with suspected BAC, the guideline developers recommend that a surgical biopsy be used to establish a histopathologic diagnosis. **Grade of recommendation, 1C**
3. For patients who are unable to undergo surgical biopsy, the diagnosis of BAC should be made only with compatible histopathologic pattern on transbronchial or core needle biopsy and a computed tomography (CT) demonstrating a pure ground-glass or pneumonic appearance. **Grade of recommendation, 1C**

4. For patients whose CT scans show ground-glass attenuation or pneumonic consolidation (suggesting BAC), positron emission tomography (PET) scans often have false-negative results, and therefore the guideline developers recommend that a PET scan with negative results be followed by additional diagnostic testing to exclude the presence of cancer. **Grade of recommendation, 1C**
5. In patients who have suspected BAC and are good surgical candidates, a sublobar resection may be appropriate, provided that the CT scan shows a pure ground-glass appearance, intraoperative pathologic consultation confirms pure BAC without evidence of invasion, and surgical margins are free of disease. **Grade of recommendation, 1B**
6. For patients with good performance status (PS) and unresectable BAC, the guideline developers recommend the use of standard chemotherapy. The use of first-line epidermal growth factor receptor (EGFR)-targeted agents should be reserved for patients with poor PS or those who are enrolled in clinical trials. **Grade of recommendation, 2C**

### **Definitions:**

#### **Quality of Evidence Scale**

**High** - Randomized controlled trials (RCTs) without important limitations or overwhelming evidence from observational studies\*

**Moderate** - RCTs with important limitations (inconsistent results, methodologic flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies\*

**Low or very low** - Observational studies or case series

\*Although the determination of magnitude of the effect based on observational studies is often a matter of judgment, the guideline developers offer the following suggested rule to assist this decision: a large effect would be a relative risk  $> 2$  (risk ratio  $< 0.5$ ) [which would justify moving from weak to moderate], and a very large effect is a relative risk  $> 5$  (risk ratio  $< 0.2$ ) [which would justify moving from weak to strong]. There is some theoretical justification in the statistical literature for these thresholds (the magnitude of effect that is unlikely or very unlikely to be due to residual confounding after adjusted analysis). However, once the decision is made, authors should be explicit in justifying their decisions.

#### **Grade of Recommendations Scale**

| <b>Grade</b> | <b>Recommendation</b> |
|--------------|-----------------------|
| 1A           | Strong                |
| 1B           | Strong                |
| 1C           | Strong                |
| 2A           | Weak                  |
| 2B           | Weak                  |
| 2C           | Weak                  |

#### **Relationship of Strength of the Supporting Evidence to the Balance of Benefits to Risks and Burdens**

| Balance of Benefits to Risks and Burdens |                                 |                                 |                 |           |
|--|---------------------------------|---------------------------------|-----------------|-----------|
| Quality of Evidence                      | Benefits Outweigh Risks/Burdens | Risks/Burdens Outweigh Benefits | Evenly Balanced | Uncertain |
| High                                     | 1A                              | 1A                              | 2A              |           |
| Moderate                                 | 1B                              | 1B                              | 2B              |           |
| Low or very low                          | 1C                              | 1C                              | 2C              | 2C        |

#### CLINICAL ALGORITHM(S)

None provided

#### EVIDENCE SUPPORTING THE RECOMMENDATIONS

##### TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

#### BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

##### POTENTIAL BENEFITS

Appropriate diagnosis and treatment of bronchioloalveolar carcinoma (BAC)

##### POTENTIAL HARMS

Not stated

#### IMPLEMENTATION OF THE GUIDELINE

##### DESCRIPTION OF IMPLEMENTATION STRATEGY

The publication of the *Diagnosis and Management of Lung Cancer: ACCP Evidence-Based Clinical Practice Guidelines; Second Edition* in *CHEST* is the first of two dissemination vehicles. The circulation of the journal is 23,000 subscribers and libraries, including six translations and distribution to 107 countries. All subscribers received a copy of this full-text guideline. The American College of Chest Physicians (ACCP) Clinical Resource on Lung Cancer is composed of a printed publication and an accompanying CD-ROM, containing a quick reference guide for physicians and other health-care providers, patient-targeted educational materials, and a set of slides for use in educational or clinical contexts. In addition, the recommendations and grading are personal digital assistant downloadable from the clinical resource. This product is available for purchase from the ACCP. The patient education materials are accessible free of charge on [www.chestnet.org](http://www.chestnet.org).



The implementation and translation of evidence-based clinical practice guidelines facilitates knowledge uptake, critical for practice change, and should ultimately lead to better patient-focused care. The HSP Subcommittee on Implementation has proposed to collaborate with the Governors, Thoracic Oncology Network, and other groups within the ACCP to disseminate and implement the guidelines in their local communities. Residency and specialty training programs are encouraged to use the guidelines in journal clubs and grand rounds. Other organizations that were invited to send representatives to the final conference and review the proposed drafts were also requested to endorse the guidelines and market them to their membership through their own communication channels.

## **IMPLEMENTATION TOOLS**

Patient Resources  
Resources

For information about [availability](#), see the "Availability of Companion Documents" and "Patient Resources" fields below.

## **INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES**

### **IOM CARE NEED**

Living with Illness

### **IOM DOMAIN**

Effectiveness  
Patient-centeredness

## **IDENTIFYING INFORMATION AND AVAILABILITY**

### **BIBLIOGRAPHIC SOURCE(S)**

Arenberg D, American College of Chest Physicians. Bronchioloalveolar lung cancer: ACCP evidence-based clinical practice guidelines (2nd edition). Chest 2007 Sep;132(3 Suppl):306S-13S. [63 references] [PubMed](#)

### **ADAPTATION**

Not applicable: The guideline was not adapted from another source.

### **DATE RELEASED**

2007 Sep

### **GUIDELINE DEVELOPER(S)**

American College of Chest Physicians - Medical Specialty Society

## **SOURCE(S) OF FUNDING**

American College of Chest Physicians

## **GUIDELINE COMMITTEE**

American College of Chest Physicians (ACCP) Expert Panel on Lung Cancer Guidelines

## **COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE**

*Primary Author:* Douglas Arenberg, MD, FCCP

## **FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST**

Funding for both the evidence review and guideline development was supported by educational grants from AstraZeneca LP, Bristol-Myers Squibb Company, Eli Lilly and Company, Genentech, and Sanofi-Aventis. Representatives from these companies were neither granted the right of review, nor were they allowed participation in any portion of the guideline development process. This precluded participation in either conference calls or conferences. No panel members or ACCP reviewers were paid any honoraria for their participation in the development and review of these guidelines.

The ACCP approach to the issue of potential or perceived conflicts of interest established clear firewalls to ensure that the guideline development process was not influenced by industry sources. This policy is published on the ACCP Web site at [www.chestnet.org](http://www.chestnet.org). All conflicts of interest within the preceding 5 years were required to be disclosed by all panelists, including those who did not have writing responsibilities, at all face-to-face meetings, the final conference, and prior to submission for publication. The most recent of these conflict of interests are documented in this guideline Supplement. Furthermore, the panel was instructed in this matter, verbally and in writing, prior to the deliberations of the final conference. Any disclosed memberships on speaker's bureaus, consultant fees, grants and other research monies, and any fiduciary responsibilities to industry were provided to the full panel in writing at the beginning of the conference and at submission for publication.

## **ENDORSER(S)**

American Association for Bronchology - Disease Specific Society  
American Association for Thoracic Surgery - Medical Specialty Society  
American College of Surgeons - Medical Specialty Society  
American Society for Therapeutic Radiology and Oncology  
Asian Pacific Society of Respiriology - Disease Specific Society  
Oncology Nursing Society - Professional Association  
Society of Thoracic Surgeons - Medical Specialty Society  
World Association of Bronchology - Disease Specific Society

## **GUIDELINE STATUS**

This is the current release of the guideline.

## **GUIDELINE AVAILABILITY**

Electronic copies: Available to subscribers of [Chest - The Cardiopulmonary and Critical Care Journal](#).

Print copies: Available from the American College of Chest Physicians, Products and Registration Division, 3300 Dundee Road, Northbrook IL 60062-2348.

## **AVAILABILITY OF COMPANION DOCUMENTS**

The following are available:

Executive Summary:

- Alberts MW. Diagnosis and management of lung cancer executive summary. Chest 2007 Sep;132(3 Suppl):1S-19.

Background Articles:

- Alberts WM. Introduction: diagnosis and management of lung cancer. Chest 2007 Sep;132(3 Suppl):20S-22.
- McCrory DC, Lewis SZ, Heitzer J, Colice GL, Alberts WM. Methodology for lung cancer evidence review and guideline development. Chest 2007 Sep;132(3 Suppl):23S-28.
- Alberg AJ, Ford JG, Samet JM. Epidemiology of lung cancer. Chest 2007 Sep;132(3 Suppl):29S-55.

Electronic copies: Available to subscribers of [Chest - The Cardiopulmonary and Critical Care Journal](#).

Print copies: Available from the American College of Chest Physicians, Products and Registration Division, 3300 Dundee Road, Northbrook IL 60062-2348.

The following is also available:

- ACCP clinical resources: Diagnosis and management of lung cancer: ACCP evidence-based clinical practice guidelines (2nd edition).

Available from the [American College of Chest Physicians Web site](#).

## **PATIENT RESOURCES**

The following are available:

- Lung cancer guides: lung cancer...am I at risk? Patient education guide. Northbrook (IL): American College of Chest Physicians, 2004. 12 p.

- Lung cancer guides: What if I have a spot on my lung? Do I have cancer? Patient education guide. Northbrook (IL): American College of Chest Physicians, 2004. 16 p.
- Lung cancer guides: living with lung cancer. Patient education guide. Northbrook (IL): American College of Chest Physicians, 2004. 12 p.
- Lung cancer guides: advanced lung cancer: issues to consider. Patient education guide. Northbrook (IL): American College of Chest Physicians, 2004. 12 p.

Electronic copies: Available in Portable Document Format (PDF) from the [American College of Chest Physicians \(ACCP\) Web site](#).

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

## **NGC STATUS**

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